What is claimed:

1. A method for detecting the presence or absence of a first nucleotide, at a position within a strand of DNA in a sample, comprising:

forming an admixture of a primer and said strand of DNA in said sample and imposing hybridization conditions on said primer and said DNA strand to form a hybridization product, said primer comprising a sequence of DNA which hybridizes with said strand of DNA adjacent to said first nucleotide position and having a second nucleotide opposite said first nucleotide position, said second nucleotide associated with a detectable label, said second nucleotide hybridizing to said first nucleotide in the event said second nucleotide is complementary to said first nucleotide and said second nucleotide not hybridizing to said first nucleotide in the event of said second nucleotide is not complementary;

applying a proofreading polymerase to the hybridization product under conditions in which said second nucleotide is preferentially excised to form a fluorescently labeled nucleotide product in the event said second nucleotide is not hybridized to said first nucleotide, and in which said second nucleotide is preferentially incorporated into an extension product in the event said second nucleotide is hybridized to said first nucleotide;

monitoring said sample for the presence of a fluorescent label in association with at least one of said fluorescently labeled nucleotide excision product, said extension product, or said primer using fluorescent polarization, which fluorescent label associated with an excess of said nucleotide excision product is indicative of the absence of said first nucleotide, and which fluorescent label associated with an excess of said extension product is indicative of the presence of said first nucleotide.

2. A method for detecting the presence or absence of a first nucleotide, at a position within a strand of DNA in a sample, comprising:

forming an admixture of a primer and said strand of DNA in said sample and imposing hybridization conditions on said primer and said DNA strand to form a hybridization product, said primer comprising a sequence of DNA which hybridizes with said strand of DNA adjacent to said first nucleotide position and having a second nucleotide opposite said first nucleotide position, said second nucleotide associated with a mass-tag, said second nucleotide hybridizing to said first nucleotide in the event said second nucleotide is complementary to said first nucleotide and said second nucleotide not hybridizing to said first nucleotide in the event of said second nucleotide is not complementary;

applying a proofreading polymerase to the hybridization product under conditions in which said second nucleotide is preferentially excised to form a nucleotide excision product attached to a mass-tag in the event said second nucleotide is not hybridized to said first nucleotide, and in which said second nucleotide is preferentially incorporated into an extension product in the event said second nucleotide is hybridized to said first nucleotide;

monitoring said sample for the presence of a mass-tag in association with at least one of said nucleotide excision product, said extension product, or said primer using mass spectrometry, which mass-tag associated with said nucleotide excision product in concentrations greater than background is indicative of the absence of said first nucleotide, and which mass-tag associated with said extension product in concentrations greater than background is indicative of the presence of said first nucleotide.

3. A method for detecting the presence or absence of a first nucleotide, at a position within a strand of DNA in a sample, comprising:

forming an admixture of a primer and said strand of DNA in said sample and imposing hybridization conditions on said primer and said DNA strand to form a hybridization product, said primer comprising a sequence of DNA which hybridizes with said strand of DNA adjacent to said first nucleotide position and having a second nucleotide opposite said first nucleotide position, said second nucleotide associated with a label, said second nucleotide hybridizing to said first nucleotide in the event said second nucleotide is complementary to said first nucleotide and said second nucleotide not hybridizing to said first nucleotide in the event said second nucleotide is not complementary;

applying a proofreading polymerase to the hybridization product under conditions in which said second nucleotide is preferentially excised to form a labeled nucleotide product in the event said second nucleotide is not hybridized to said first nucleotide, and in which said second nucleotide is preferentially incorporated into an extension product in the event said second nucleotide is hybridized to said first nucleotide;

providing a dialysis chamber having a dialysis membrane with a molecular weight cut-off such that the labeled nucleotide excision product, the primer, and the extension product may pass through at substantially different rates;

providing a means for introducing the admixture into a chamber on a first side of the dialysis membrane, and for introducing a dialysis solution into a chamber on a second side of the dialysis membrane opposite the first side of the dialysis membrane;

monitoring the sample on the first side of the dialysis membrane, or monitoring the dialysis solution on the second side of the dialysis membrane, or both, for the presence of a label;

the presence of a label in the dialysis solution in concentrations greater than background after a short time is indicative of the absence of the first nucleotide, and the presence of a label remaining in the sample chamber in concentrations greater that background after a long time is indicative of the presence of the first nucleotide.

4. A method for detecting the presence or absence of a first nucleotide, at a position within a strand of DNA in a sample, comprising:

forming an admixture of a primer, said strand of DNA in said sample, and a mixture of labeled dideoxynucleotides, said primer comprising a sequence of DNA which hybridizes with said strand of DNA adjacent to said first nucleotide position and having a second nucleotide opposite said first nucleotide position which is not complementary to said first nucleotide;

imposing hybridization conditions on said primer and said DNA strand to form a hybridization product;

applying a proofreading polymerase to the hybridization product under conditions in which said second nucleotide is excised and a labeled dideoxynucleotide is inserted that is complementary to said first nucleotide position; and

monitoring said sample for the presence of a label in association with at least one of said primer or said hybridization product, which label associated with said primer or said hybridization product in concentrations greater than background is indicative of the presence of said first nucleotide.

5. A method for detecting the presence or absence of a first nucleotide, at a position within a strand of DNA in a sample, comprising:

forming an admixture of a primer and a strand of DNA in said sample and imposing conditions such that a hybridization product is formed between the primer and said DNA strand, said primer comprising a sequence of DNA which hybridizes with the strand of DNA and having a second nucleotide containing a fluorescent label opposite the position of the first nucleotide and said primer also containing a quencher moiety attached at a position adjacent to the second nucleotide, the second nucleotide hybridizing to the first nucleotide in the event that the second nucleotide is complementary to the first nucleotide and the second nucleotide not hybridizing to the first nucleotide in the event that the second nucleotide is not complementary;

applying a proofreading polymerase to the hybridization product under conditions in which the second nucleotide containing the fluorophore is preferentially excised in the event that the second nucleotide is not hybridized to the first nucleotide and in which the second nucleotide containing the fluorophore is preferentially incorporated into primer extension product in the event that the second nucleotide is hybridized to the first nucleotide;

monitoring the sample for emission from the fluorophore, the presence of fluorescence emission at levels greater than background being indicative of the absence of the first nucleotide, and the absence of fluorescence emission being indicative of the presence of the first nucleotide.

6. The method of claim 5, wherein said quencher moiety is attached about 1-10 nucleotides away from the position of the fluorescent label on said second nucleotide opposite said first nucleotide when said primer and said DNA sample are paired.

7. The method of claim 5, wherein said fluorophore is a fluorescent label having an absorption maximum in a wavelength range between 340 nm and 820 nm and an emission maximum in a wavelength range between 370 nm and 850 nm.

8. The method of claim 5, wherein said fluorophore is a fluorescent label selected from the group consisting of: Alexa Fluor 350, Alexa Fluor 488, Alexa Fluor 532, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, Alexa Fluor 633, Alexa Fluor 660 and Alexa Fluor 680, AMCA, AMCA-S, BODIPY FL, BODIPY R6G, BODIPY TMR, BODIPY TR, BODIPY 530/550, BODIPY 558/568, BODIPY 564/570, BODIPY 576/589, BODIPY 581/591, BODIPY 630/650, BODIPY 650/665, Carboxyrhodamine 6G, carboxy-X-rhodamine (ROX), Cascade Blue, Cascade Yellow, Cy3, Cy5, Cy3.5, Cy5.5, Dansyl, Dapoxyl, Dialkylaminocoumarin, 4',5'-Dichloro-2',7'-dimethoxy-fluorescein, DM-NERF, Eosin, Erythrosin, Fluorescein, FAM, Hydroxycoumarin, IRD40, IRD 700, IRD 800, JOE, Lissamine rhodamine B, Marina Blue, Methoxycoumarin, Naphthofluorescein, Oregon Green 488, Oregon Green 500, Oregon Green 514, Pacific Blue, PyMPO, Pyrene, Rhodamine 6G, Rhodamine Green, Rhodamine Red, Rhodol Green, 2',4',5',7'-Tetra-bromosulfone-fluorescein, Tetramethyl-rhodamine (TMR), Carboxytetramethylrhodamine (TAMRA), Texas Red, and Texas Red-X.

9. The method of claim 5, wherein said quencher moiety displays a Förster radius of greater than 30 Ångstroms when paired with a fluorophore under conditions where FRET may occur, and having a broad absoption spectrum with an absorption maximum in the range of 480-700 nm.

10. The method of claim 5, wherein said quencher moiety is selected from the group consisting of DABCYL, QSY-7, QSY-33, Q1, BHQ-1, BHQ-2, and BHQ-3.

11. A method for detecting the presence or absence of a first nucleotide, at a position within a strand of DNA in a sample, comprising:

forming an admixture of a primer and a strand of DNA in said sample and imposing conditions such that a hybridization product is formed between the primer and said DNA strand, said primer comprising a sequence of DNA which hybridizes with the strand of DNA and having a second nucleotide containing a quencher opposite the position of the first nucleotide and said primer also containing a fluorescent label attached at a position adjacent to said second nucleotide, the second nucleotide hybridizing to the first nucleotide in the event that the second nucleotide is complementary to the first nucleotide and the second nucleotide not hybridizing to the first nucleotide in the event that the second nucleotide is not complementary;

applying a proofreading polymerase to the hybridization product under conditions in which the second nucleotide containing the quencher is preferentially excised in the event that the second nucleotide is not hybridized to the first nucleotide and in which the second nucleotide containing the quencher is preferentially incorporated into primer extension product in the event that the second nucleotide is hybridized to the first nucleotide;

monitoring the sample for emission from the fluorophore, the presence of fluorescence emission at levels greater than background being indicative of the absence of the first nucleotide, and the absence of fluorescence emission being indicative of the presence of the first nucleotide.

12. The method of claim 11, wherein said quencher moiety is attached about 1-10 nucleotides away from the position of the fluorescent label on said second nucleotide opposite said first nucleotide when said primer and said DNA sample are paired.

13. The method of claim 11, wherein said fluorophore is a fluorescent label having an absorption maximum in a wavelength range between 340 nm and 800 nm and

an emission maximum in a wavelength range between 400 nm and 850 nm.

14. The method of claim 11, wherein said fluorophore is a fluorescent label selected from the group consisting of: Alexa Fluor 350, Alexa Fluor 488, Alexa Fluor 532, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, Alexa Fluor 633, Alexa Fluor 660 and Alexa Fluor 680, AMCA, AMCA-S, BODIPY FL, BODIPY R6G, BODIPY TMR, BODIPY TR, BODIPY 530/550, BODIPY 558/568, BODIPY 564/570, BODIPY 576/589, BODIPY 581/591, BODIPY 630/650, BODIPY 650/665, Carboxyrhodamine 6G, carboxy-X-rhodamine (ROX), Cascade Blue, Cascade Yellow, Cy3, Cy5, Cy3.5, Cy5.5, Dansyl, Dapoxyl, Dialkylaminocoumarin, 4',5'-Dichloro-2',7'-dimethoxy-fluorescein, DM-NERF, Eosin, Erythrosin, Fluorescein, FAM, Hydroxycoumarin, IRD40, IRD 700, IRD 800, JOE, Lissamine rhodamine B, Marina Blue, Methoxycoumarin, Naphthofluorescein, Oregon Green 488, Oregon Green 500, Oregon Green 514, Pacific Blue, PyMPO, Pyrene, Rhodamine 6G, Rhodamine Green, Rhodamine Red, Rhodol Green, 2',4',5',7'-Tetra-bromosulfone-fluorescein, Tetramethyl-rhodamine (TMR), Carboxytetramethylrhodamine (TAMRA), Texas Red, and Texas Red-X.

15. The method of claim 11, wherein said quencher moiety displays a Förster radius of greater than 30 Ångstroms when paired with a fluorophore under conditions where FRET may occur, and having a broad absoption spectrum with an absorption maximum in the range of 480-700 nm.

16. The method of claim 5, wherein said quencher moiety is selected from the group consisting of DABCYL, QSY-7, QSY-33, Q1, BHQ-1, BHQ-2, and BHQ-3.

17. A method for detecting the presence or absence of a first nucleotide, at a position within a strand of DNA in a sample, comprising:

forming an admixture of a primer and a strand of DNA in said sample and imposing conditions such that a hybridization product is formed between the primer and said DNA strand, said primer comprising a sequence of DNA which hybridizes with the strand of DNA and having a second nucleotide containing an electrophoretic tag (e-tag) moiety opposite the position of the first nucleotide, the second nucleotide hybridizing to the first nucleotide in the event that the second nucleotide is complementary to the first nucleotide and the second nucleotide not hybridizing to the first nucleotide in the event that the second nucleotide is not complementary;

applying a proofreading polymerase to the hybridization product under conditions in which the second nucleotide containing the e-tag is preferentially excised in the event that the second nucleotide is not hybridized to the first nucleotide and in which the second nucleotide containing the e-tag is preferentially incorporated into primer extension product in the event that the second nucleotide is hybridized to the first nucleotide;

monitoring the sample for the presence of e-tag labeled nucleotide products by electrophoretic separation, the presence of such e-tag nucleotide products at levels greater than background being indicative of the absence of the first nucleotide, and the absence of such e-tag nucleotide products being indicative of the presence of the first nucleotide.

18. The method of any one of claims 1, 2, 3, 5, 11, or 17 wherein multiple nucleotide variants at the position of said first nucleotide are tested simultaneously in the same reaction vessel by using more than one labeled primer.

19. The method of any one of claims 1, 2, 3, 5, 11, or 17 wherein multiple nucleotide variants from different genetic loci are tested simultaneously in the same reaction vessel by using more than one labeled primer.

20. The method of any one of claims 1, 2, 3, 4, 5, 11, or 17 wherein the amount of said nucleotide excision product and of said extension product are increased by means of an amplification reaction that results in faithful replication of said DNA strand in the sample.

21. The method of any one of claims 1, 2, 3, 5, 11, or 17 wherein the amount of said nucleotide excision product and of said extension product are increased by means of polymerase chain reaction (PCR) amplification in the presence of a reverse primer.

22. The method of any one of claims 1, 2, 3, 5, 11, or 17 wherein the amount of said nucleotide excision product and of said extension product are increased by means of a linear amplification reaction, such as a cycled hybridization and extension reaction.

23. The method of any one of claims 1, 2, 3, 5, 11, or 17 wherein the amount of said nucleotide excision product and said extension product is amplified by means of rolling circle amplification (RCA) after circularization of said DNA strand in the sample.

24. The method of any one of claims 1, 2, 3, 4, 5, 11, or 17 wherein said DNA of the sample is genomic DNA.

25. The method of any one of claims 1, 2, 3, 4, 5, 11, or 17 wherein said primer further comprises a tail that is non-complementary with said DNA strand.

26. The method of claim 2, wherein said mass-tag comprises an electrophore mass-tag and said mass spectrometry is electron-capture mass spectrometry.

27. The method of claim 2, wherein said mass-tag is a nucleotide or an oligonucleotide, and said mass spectrometry is matrix-assisted laser desorption/ionization time-of-flight mass spectrometry.

28. The method of claim 2, wherein said mass-tag is an organic molecule with a molecular weight between 100 and 2000 Daltons.

29. The method of claim 3, wherein said dialysis membrane comprises a semi-permeable microfiber.

30. The method of claim 3, wherein said dialysis occurs in a microfluidic channel in the absence of a semi-permeable membrane.

31. The method of claim 3, wherein said dialysis chamber has a molecular weight cut-off of about 100 KDa.

32. The method of claim 17, wherein said electrophoretic separation occurs in a polymer filled capillary or microchannel.

33. A method for determining allele frequency at a first nucleotide position within a strand of DNA in a sample, comprising:

providing a first primer, said first primer comprising a sequence of DNA which hybridizes with said strand of DNA adjacent to said first nucleotide position, and having a second nucleotide opposite said first nucleotide position, said second nucleotide associated with a first detectable label, said second nucleotide hybridizing to said first nucleotide in the event said second nucleotide is complementary to said first nucleotide and said second nucleotide not hybridizing to said first nucleotide in the event said second nucleotide is not complementary;

providing a second primer, said second primer comprising a sequence of DNA which hybridizes with said strand of DNA adjacent to said first nucleotide position, and having a third nucleotide opposite said first nucleotide position, said third nucleotide associated with a second detectable label, said third nucleotide hybridizing to said first nucleotide in the event said third nucleotide is complementary to said first nucleotide and said third nucleotide not hybridizing to said first nucleotide in the event said third nucleotide is not complementary;

forming an admixture of said first and second primers and said strand of DNA in said sample and imposing hybridization conditions on said first and second primers and said DNA strand to form a hybridization product;

applying a proofreading polymerase to the hybridization product under conditions in which said second and said third nucleotide is preferentially excised in the event said second and said third nucleotide is not hybridized to said first nucleotide, and in which said second and said third nucleotide is preferentially incorporated into an extension product in the event said second and said third nucleotide is hybridized to said first nucleotide;

monitoring said sample for the presence of a first or a second label in association with said extension product, wherein the ratio of said first and said second label is indicative of allele frequency at said first nucleotide position within a strand of DNA in a sample.